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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,715	06/18/2001	Mark Pines	CGD-004.0P-U	7532

7590 10/11/2005

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 10/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,715	PINES ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24, 25 adn 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,25 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 24, 25 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pines et al. (US 5449678 A), and further in view of Ramieres et al. (Journal of Molecular and

Cellular Cardiology, 1998, abstract, 30(3), pp. 475-83) and Crawford et al. (Circulation Research, 1994, abstract, (4), pp. 727-39).

Pines'678 teaches the use of quinazolinone containing composition (e.g., halofuginone) for treating or preventing fibrotic disorders such as myocardial fibrosis by inhibiting collagen type I synthesis (col. 5, lines 13-16; col. 6, line 4). The reference also teaches that halofuginone inhibits collagen type I synthesis at transcription level, regardless of the tissue or animal species (column 22, lines 23-26).

Ramieres et al. (Journal of Molecular and Cellular Cardiology, 1998, abstract, 30(3), pp. 475-83) and Crawford et al. (Circulation Research, 1994, abstract, (4), pp. 727-39) are being supplied herein to demonstrate that the chronic administration of angiotensin II leads to myocardial fibrosis and animal models for the disease are known in the art.

As discussed above, although Pine's 678 teaches the utility of halofuginone in inhibiting collagen type I synthesis, thereby treating or preventing myocardial fibrosis, the reference does not specifically state that the subject exposed to the promoter of cardiac fibrosis such as the elevated angiotensin II, particularly prior to the subject exhibits a cardiac fibrotic condition, is susceptible to the administration of said composition. However, one having ordinary skill in the art at the time of the invention was made would have known that the enhanced activity of angiotensin II induces mycocardial fibrosis in animal and myocardial fibrosis can be generated in lab animals in several ways including the administration of angiotension II. Thus, one having ordinary skill in the art would have expected that the subject has been exposed to the chronic administration of angiotensin II would be benefited from the administration of halofuginone, for the ultimate purpose of treating or preventing myocardial fibrosis.

As discussed above, the prior art does not disclose that whether the administration of said composition is useful in the subject exposed to the promoter of cardiac fibrosis such as the elevated angiotensin II, particularly before the subject exhibits a cardiac fibrotic condition. However, the fact that the applicant may have discovered treatment recipient group, namely "the subject has been exposed to a promoter of cardiac fibrosis and the step of administering the compound is before the subject exhibits a cardiac fibrotic condition", is not considered patentably distinctive over the prior art which are directed to the same ultimate therapeutic application (for the treatment or prevention of myocardial fibrosis).

Response to Arguments

2. Applicant's arguments filed July 05,2005 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that Pines, based merely on its effects on avian skin fibroblasts and chondrocytes, does not provide a reasonable expectation of success that administration of halofuginone to a patient would effectively prevent and/or treat cardiac fibrosis. Applicant alleges that there is no correlation between in vitro experiments and a practical utility in the treatment or prevention of cardiac fibrosis.

This argument is not found persuasive. Unlike the applicant's argument, Pines teaches that the halofuginone inhibits collagen type I synthesis at transcription level, regardless of the tissue or animal species (see column 3, line 65 thru column 4, line 4 and column 22, lines 23-26). Furthermore, Pines teaches that the halofuginone is useful in the treatment/prevention of fibrotic condition associated with the increased collagen type I synthesis including myocardial fibrosis (column 6, lines 3-4).

Abnormal increased collagen type I synthesis is involved in pathogenesis of various fibrotic conditions including myocardial fibrosis (Querejeta et al., Circulation, 2004;110) and chronic graft-versus-host disease and scleroderma (Pines et al., Biology of Bood and Marrow Transplantation, 2003, abstract, Vol. 9, Issue 7, pp. 417-425). Thus, reading the whole context of Pines, the skilled artisan would have expected that the the halofuginone, known inhibitor of collagen type I synthesis at transcription level, regardless of the tissue or animal species, is useful in the treatment/prevention of collagen type I associated fibrosis such as myocardial fibrosis or cardiac fibrosis.

Conclusion

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. No Claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614

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